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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/761,893	01/17/2001	Shih-Chieh Hung	11709-003001	6011

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EXAMINER	
GARVEY, TARA L	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/761,893	HUNG ET AL.	
	Examiner	Art Unit	
	Tara L. Garvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6,7,9-11,23 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6,7,9-11 and 32* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 4, 6, 7, 9-20, 23 and 32 are pending.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 14, 2006 has been entered.

Non-Compliant Amendment

The text of "withdrawn" claims 12-20 is required to be present in the claims listing. See MPEP 714 [R-3], section IIC under the heading Amendments to Claims. Please provide a new listing of claims.

Response to Arguments

Applicant's arguments, filed March 24, 2006, with respect to the written description rejection made on July 15, 2005 and maintained on December 15, 2005 have been fully considered and are persuasive: The rejection of claims 1, 4, 6, 7, 9-11, 23 and 32 has been withdrawn with regard to this written description rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicant's arguments filed March 24, 2006 have been fully considered but they are not fully persuasive.

Claims 1, 4, 6, 7, 9-11, 23 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This maintains the new matter rejection. The response below addresses the arguments with respect to new matter.**

Applicant argues that narrowing the pore size to "0.4 to 20 micron" is of course within the range of 0.4 to 40 microns and that the examiner did not respond to the previous evidence presented by the applicant from MPEP 2163.06. The previous arguments are that the MPEP states that "information contained in any one of the specification, claims or drawings of the application as filed may be added to any other part of the application without introducing new matter." Further, the applicant argued that the case law cited in the MPEP does not require a description of the subject matter in "ipsis verbis" nor does it require a specific example (i..e. Heymes v. Takaya) and that

the written description rules are in appropriately applied to narrowed claims involving ranges (In re Wertheim and Hilton Davis Chemical Co. v. Waner-Jenkinson Company, Inc.) Finally, the applicant concludes that narrowing the claim within the original scope shall not constitute new matter.

In response to applicant's arguments, the newly claimed narrower range is encompassed by the broader range that is described in the specification, but claiming the narrower range still constitutes new matter because the narrow range was not originally taught in the specification. In terms of the statement from MPEP 2163.06, the interpretation of this section is that information that is already contained in the disclosure can be added to another part of the disclosure without introducing new matter, but if the information is not already contained in any part of the disclosure, then the addition of the information would constitute new matter. In the Heymes v. Takaya decision, the applicant concludes that in order to comply with the written description requirement, the applicant does not have to provide a description of the subject matter or a specific example. Although these items are not required, the applicant must provide enough information in the specification to convey that they were in possession of the claimed invention at the time of filing. The case of Hilton Davis Chemical Co. v. Warner-Jenkinson Company was not discussed in MPEP 2163.06, but was rather discussed in MPEP 2183 and was a case based on a primia facie case of equivalence. The examiner is unclear as to the conclusions being drawn by this case decision in terms of written description at it relates to new matter. In terms of the applicant's interpretation of In re Wertheim case, the examiner does not agree. This case

demonstrated that narrowing the claims when there is no support in the originally filed disclosure is a violation of written description. The applicant is directed to MPEP 2163.05 for examples of the relationship between claimed ranges and the written description requirement. Excerpts from this section serving as examples are the following: (a) The failure to meet the written description requirement of 35 U.S.C. 112, first paragraph, commonly arises when the claims are changed after filing to either broaden or narrow the breadth of the claim limitations, or to alter a numerical range limitation or to use claim language which is not synonymous with the terminology used in the original disclosure. To comply with the written description requirement of 35 U.S.C. 112, para. 1, or to be entitled to an earlier priority date or filing date under 35 U.S.C. 119, 120, or 365(c), each claim limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure. See MPEP § 2163 for examination guidelines pertaining to the written description requirement. (b) The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g.,Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir.1996) (a "laundry list" disclosure of every possible moiety does not constitute a writtendescription of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species). (c) With respect to changing numerical range limitations, the analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure. In the decision in In re Wertheim,

541 F.2d 257, 191 USPQ 90 (CCPA 1976), the ranges described in the original specification included a range of"25%- 60%" and specific examples of "36%" and "50%." A corresponding new claim limitation to "at least 35%" did not meet the description requirement because the phrase "at least" had no upper limit and caused the claim to read literally on embodiments outside the "25% to 60%" range, however a limitation to "between 35% and 60%" did meet the description requirement. The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir.1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species).

Claims 1, 4, 6, 7, 9-11, 23 and 32 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record as set forth in the office action mailed December 16, 2005, the Advisory Action mailed February 22, 2006 and above.

New Grounds of Rejection

Claim Objections

Claim 9 is objected to because of the following informalities: The phrase "the mesenchymal stem cells are differentiable" is awkward. Please change the phrase to "the mesenchymal stem cells can differentiate". Appropriate correction is required.

Claim 23 is objected to because of the following informalities: Claim 23 is dependent from canceled claim 5. Please rewrite claim 23 in independent form to include the limitations from the canceled parent claim. Claim 23 was examined based on the limitation set forth in claim 5. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 4, 6, 7, 9-11 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for recovering mesenchymal stem cells from bone marrow, does not reasonably provide enablement for recovery of mesenchymal stem cells from any source. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art, relative skill in the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claim, with the most relevant discussed below.

Nature of the invention: The claims are directed to a method of isolating mesenchymal stem cells from a mixture of cells using a culture device comprised of a porous plate that allows mesenchymal stem cells (MSCs) to remain in the upper portion of the culture device and to then adhere to the upper plate of the device.

Breadth of the claim: The claim is broad in that it reads on porous plate with no definitive pore size that will allow for the recovery of mesenchymal stem cells from a cell mixture obtained from any source.

Guidance in the specification/Existence of a working example: The specification describes a method of separating MSCs from a cell mixture using a culture device with a porous plate, which will allow MSCs to remain in the upper portion of the culture device and eventually adhere to the upper plate from which they can be collected. In addition, the specification describes the porous plate will have a pore size range of 0.4 to 40 microns. The working example provided in the specification demonstrates the recovery of population of mesenchymal stem cells from bone marrow that is 98% pure. The specification further demonstrates that the mesenchymal stem cells obtained from bone marrow have the ability to differentiate into osteogenic, adipogenic and

chondrogenic cell lineages and are characterized as negative for CD14, CD34, CD38, CD50 and CD120a expression with a low level of CD29 expression.

The specification has not described what cells in addition to mesenchymal stem cells may adhere to the plate when a cell mixture other than that obtained from bone marrow is used in the claimed invention. Since many types of cells, other than MSC, have the ability to adhere to a tissue culture plate, it is unlikely that the cell culture device described will only allow MSCs to adhere to the plate when a cell mixture other than bone marrow is used. Additionally, the specification does not describe a specific pore size that will allow only MSCs to remain in the upper portion of the culture device when cell mixtures obtained from various sources are applied to the culture device. A pore size range of 0.4 to 40 microns may allow many other cells besides MSCs to remain on the upper plate when a cell mixture obtained from a source other than bone marrow is applied to the culture device. Further, the specification describes on page 8, line 28 to page 9, line 4, that the bone marrow is seeded into the culture device with a pore size ranging from 0.4 to 40 microns so that small-size hematopoietic cells can pass through the pores to the bottom plate, but the specification has not taught a cell type that will be able to pass through a pore size of 0.4 μM since the smallest circulating blood cell is 1.5 μM as evidence by Burkitt et al (Wheater's Functional Histology (1993), page 60, see Figure 3.17).

State of the art/Predictability of the art: The state of the art describes that MSC have a large size (Van Vlasselaer et al, Blood, 1994, page 758, right column, first full paragraph bridging to page 759; cited in the office action mailed on July 15, 2005).

Further, the art describes the size of blood cells ranging from 1.5 μM to 20 μM (Burkitt et al (Wheater's Functional Histology (1993), page 60, see Figure 3.17). The art does not describe a cell type that is small enough to pass through a pore size of 0.4 microns a size range that would encompass the size of mesenchymal stem cells. Thus, the art is unpredictable as to the pore size that would be sufficient in the selection of a pure population of only mesenchymal stem cells from a cell mixture obtained from a variety of sources.

Quantity of experimentation: A large amount of experimentation would be required to determine the pore size of the culture device and culture conditions that would only allow MSCs to remain in and adhere to the upper portion of the culture device when various cell mixtures isolated from a variety of sources such an embryonic yolk sac, a placenta, umbilical cord blood, any fetal or adult tissue or any fetal or adult body fluid are applied to the culture device.

Conclusion: In order to practice the claimed invention, the skilled artisan would not have found sufficient guidance in the specification or the prior art to make and use a culture device containing a porous plate with the proper material and pore size to select for MSCs from any cell source other than bone marrow. The skilled artisan would have had to engage in a large amount of experimentation to make and use the claimed invention. In view of the lack of guidance in the specification and the large amount of experimentation in an unpredictable art, it would require undue experimentation to practice the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tara L Garvey whose telephone number is (571) 272-2917. The examiner can normally be reached on Monday through Friday 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a

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Tara L Garvey
Examiner
Art Unit 1636

TLG

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